

July 2, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Cohn, et al  
Serial No. Unassigned  
Filed: June 29, 2001  
For: 3-PHOSPHOADENOSINE-5-PHOSPHOSULFATE (PAPS)  
SYNTHETASE PROTEINS AND METHODS FOR TREATING  
OSTEOARTHRITIC DISORDERS  
Examiner: Unassigned  
Unit: --

**PRELIMINARY AMENDMENT****CERTIFICATE OF EXPRESS MAILING**

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**JULY 2, 2001**

Date of Deposit and Signature

Ann Weiss

**EL 900688417 US**

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BOX PATENT APPLICATION  
Assistant Commissioner for Patents  
Washington, D. C. 20231

Dear Sir:

This Preliminary Amendment accompanies a divisional application of pending application Serial Number 09/399,212 filed September 17, 1999. The divisional application filed herewith is directed to Claims 41-45 and 102-108 which were designated Group IV in a restriction requirement mailed December 20, 2000. In connection with the above-captioned application, the Examiner is respectfully requested to consider the following amendments and remarks.

**AMENDMENT**

A Version With Markings To Show Changes Made is included at pages 5-7, after Applicant's Remarks.

IN THE SPECIFICATION:

In the Title, at page 1, line 1, please delete "GENETIC MARKER FOR SPONDYLOEPIMETAPHYSEAL DYSPLASIA", and insert therefor:

--3-PHOSPHOADENOSINE-5-PHOSPHOSULFATE (PAPS)  
SYNTHETASE PROTEINS AND METHODS FOR TREATING  
OSTEOARTHRITIC DISORDERS--.

At page 1, line 4, before "Background of the Invention", please insert the following:

--This application is a division of U.S. Serial No. 09/399,212 filed September 17, 1999, and is further related to U.S. Serial No. \_\_\_\_\_, filed July 2, 2001, which is a division of U.S. Serial No. 09/399,212.--.

IN THE CLAIMS:

Please cancel Claims 1-40 and 46-101, without prejudice, as being directed to designated claim Groups I, II, III and V. Please cancel Claims 41-45 and 102-108, without prejudice, and add new Claims 109-120 as follows:

-- 109. (New) An isolated PAPS synthetase protein comprising a polypeptide having an amino acid sequence of (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), or an antibody binding fragment of either of these at least 6 amino acids long.

110. (New) A PAPSS2 fusion protein, comprising:  
a first PAPSS2 polypeptide segment comprising an amino acid sequence of (SEQ. ID. NO.:7) or a gene-specific antibody binding fragment thereof at least 6 amino acids long;  
and  
a second predetermined polypeptide segment.

111. (New) The fusion protein of Claim 110, wherein the PAPSS2 polypeptide segment is encoded by a nucleic acid segment having a nucleotide sequence of (SEQ. ID. NO.:9) or a gene-specific fragment thereof.

112. (New) A Papss2 fusion protein comprising:

a first Papss2 polypeptide segment comprising an amino acid sequence of (SEQ. ID. NO.:8) or a gene-specific antibody binding fragment thereof at least 6 amino acids long; and a second predetermined polypeptide segment.

113. (New) The fusion protein of Claim 112, wherein the Papss2 polypeptide segment is encoded by a nucleic acid segment having a nucleotide sequence of (SEQ. ID. NO.:10), or a gene-specific fragment thereof.

114. (New) The PAPSS2 fusion protein of Claim 110, wherein the second polypeptide segment is an human immunodeficiency virus TAT protein.

115. (New) The PAPSS2 fusion protein of Claim 111, wherein the second polypeptide segment is an human immunodeficiency virus TAT protein.

116. (New) A protein therapy method for treating a human subject having an osteoarthritic disorder, comprising:

exposing a cell of a tissue of a human subject having an osteoarthritic disorder that is caused or aggravated by deficient enzymatic sulfation activity to a fusion protein comprising a first PAPSS2 polypeptide segment that comprises an amino acid sequence of (SEQ. ID. NO.:7), or an enzymatically active fragment thereof, and a second polypeptide segment capable of infiltrating the cell, whereby the fusion protein is taken up by the cell and the PAPSS2 polypeptide segment is enzymatically active therein.

117. (New) The protein therapy method of Claim 116, wherein the second polypeptide segment is an human immunodeficiency virus TAT protein.

118. (New) The protein therapy method of Claim 116, wherein the osteoarthritic disorder is spondyloepimetaphyseal dysplasia, Stickler syndrome, spondyloepiphyseal dysplasia, achondrogenesis, achondroplasia, chondrodysplasia, diastrophic dysplasia, pseudoachondroplasia, or multiple epiphyseal dysplasia.

119. (New) A kit for the treatment of osteoarthritic disorders caused or aggravated by deficient enzymatic sulfation activity, comprising:

a fusion protein comprising a first PAPSS2 polypeptide segment that comprises an amino acid sequence of (SEQ. ID. NO.:7), or an enzymatically active fragment thereof, and a second polypeptide segment capable of infiltrating the cell; and

instructions for using the fusion protein for treating osteoarthritic disorder(s) caused or aggravated by deficient enzymatic sulfation activity.

120. (New) The kit of Claim 119, wherein the second polypeptide segment is an human immunodeficiency virus TAT protein.--.

### REMARKS

Applicant's Preliminary Amendment is submitted together with a divisional application directed to Claims 41-45 and 102-108, originally filed in pending parent U.S. Serial No. 09/399,212 filed September 17, 1999 which claims were designated Group IV in a restriction requirement, mailed December 20, 2000.

The amendment of the title (at page 1, line 1) is to bring the title into conformity with the current claims 41-45 and 102-108, and no new matter is introduced.

Applicant believes that no new matter is introduced by any amendments made herein.

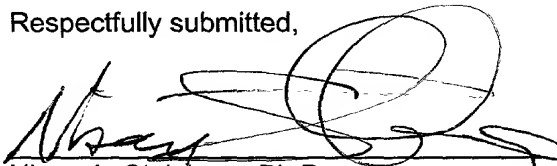
At page 1, line 3, Applicant has added continuing data explaining the relationship to U.S. Serial No. 09/399,212 filed September 17, 1999 and other related applications.

The cancellation of Claims 1-40 and 46-101, without prejudice, is made because Claims 1-40 and 46-101 were designated claim Groups I, II, III and V, and are not directed to the subject matter of the present division (i.e., Group IV).

Applicant's cancellation of Claims 41-45 and 102-108, is made without prejudice. New Claims 109-120 are added, and support is found, for example, in Claims 41-45 and 102-108, as originally filed.

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE****IN THE SPECIFICATION:**

In the Title, at page 1, line 1,

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DYSPLASIA] 3-PHOSPHOADENOSINE-5-PHOSPHOSULFATE  
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